

Response to American College of Physician's statement on the ethics of transplant after normothermic regional perfusion

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This paper responds to the position statement released by the American College of Physicians (ACP) entitled “Ethics, Determination of Death, and Organ Transplantation in Normothermic Regional Perfusion (NRP) with Controlled Donation after Circulatory Determination of Death (cDCD): American College of Physicians Statement of Concern.” The ACP’s statement engages with critical ethical issues surrounding cDCD NRP, but several of their conclusions are flawed. Contrary to the statement, the practice respects the dead donor rule and the legal definition of death while honoring the wishes of the deceased and their loved ones to help save the lives of those in need of organ transplants. cDCD NRP is well established in many countries, it can enhance trust in medical practice and organ donation, and will increase the availability of optimal organs for life-saving transplants.

KEY WORDS

donors and donation; donation after circulatory death; editorial/personal viewpoint; ethics; ethics and public policy; law/legislation; organ perfusion and preservation; organ procurement; organ procurement and allocation; organ transplantation in general

On April 17, 2021, the American College of Physicians (ACP) released a position statement on the “Ethics, Determination of Death, and Organ Transplantation in Normothermic Regional Perfusion (NRP) with Controlled Donation after Circulatory Determination of Death (cDCD): American College of Physicians Statement of Concern.”¹ The statement was published on the ACP’s website and does not include authorship or a conflict-of-interest disclosure. The ACP’s attention to this practice and engagement with related ethical issues demonstrates compassion and commitment to improving healthcare. But we believe several of their conclusions are flawed. Organ transplantation after thoracoabdominal-normothermic regional perfusion (TA-NRP) with controlled donation after circulatory death, hereafter cDCD NRP, is well established in many countries.² However, we agree there remain ethical challenges unique to the United States setting.³ These stem from how to interpret the legal definition of death, the dead donor rule, and the importance of trust

in medicine. Such challenges are surmountable in ways that continue to promote respect for the wishes of patients and their families, enhance trust in transplant and life-saving care, and expand the availability of optimal organs to save lives. A more thorough exploration of the ethical, legal, and logistical concerns regarding cDCD NRP was previously published by the *American Journal of Transplantation* last year.³ The purpose of this article is to present and respond to the key points from the ACP position statement.

It should be noted that TA-NRP is distinct from abdominal-NRP (A-NRP), in that the latter does not perfuse the heart nor any part of the body above the diaphragm. The concerns expressed in the ACP’s statement are most relevant to TA-NRP. Since the ACP statement only uses the term NRP, this article will do the same for consistency.

ACP holds that cDCD NRP violates the dead donor rule—that donors cannot be made dead to obtain their organs and that organ retrieval cannot cause death.

Abbreviations: ACP, American College of Physicians; cDCD, controlled donation after circulatory determination of death; NRP, normothermic regional perfusion.

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In cDCD NRP, the donor is declared dead in strict accordance with the legal requirements for death declaration, which will be made clear in the following section. The determination occurs prior to any organ preservation/recovery procedures. This is the same protocol as observed in any determination of death by circulatory criteria, and in standard cDCD organ donation, which has been in place for close to three decades in the United States and has saved thousands of lives. A dead donor cannot be “made” dead, nor can organ retrieval cause death in a dead body.

ACP supports cDCD without NRP because there is no intention to resuscitate the patient and auto-resuscitation is not possible (“hands-off” period is observed), which meets the “permanent” cessation of function requirements for death. ACP then says that in cDCD NRP, the intention is to restore circulation and resuscitate the patient, which violates the requirements for declaring death by circulatory criteria.

Declaring death by circulatory criteria first requires that circulation will not restart spontaneously—which is called “auto-resuscitation.” All deceased considered for cDCD NRP are subject to the “hands-off” period and thus meet this criterion. Declaring death by circulatory criteria then requires that circulation will not be restored because resuscitation efforts will not be attempted. Resuscitation efforts require attempting to restart the heart for life-saving/prolonging purposes. In undertaking cDCD NRP, there is no intention or attempt to resuscitate because doing so would be medically ineffective. Together, the family and the care team have determined that heroic support of the patient would be medically ineffective prior to the withdrawal of ventilator and pharmacological therapies. Perfusing the thoracic and abdominal organs after circulatory determination of death does not alter the fact that the heart will not restart on its own, nor does it change the fact that continued care would be medically ineffective and inconsistent with a meaningful existence. Reperfusion after cDCD for the purpose of organ donation is not therapeutic and does not change the circumstances that lead the family, in collaboration with the care team, to conclude that the possibility of a meaningful life no longer exists for the patient. cDCD NRP is wholly separate from resuscitation.

These facts do not gerrymander the definition of death any more than what takes place practically every time a patient is declared dead. The “irreversibility” requirement found in the law—circulation stops and cannot be restarted—is routinely interpreted as a “permanence” requirement—circulation stops and clinicians will not attempt to resuscitate.⁴ Without consensus on ceasing attempts to resuscitate, doctors would be prevented from declaring anyone dead according to an irreversibility standard because of the ever-present possibility of restoring some minimal amount of function for some period of time. This means it is time to update the legal definition of death to recognize the current ethical practice. Death can be declared when circulation has stopped permanently. Permanent cessation is when circulation has stopped on its own and there will be no attempt to restart it.⁵

The current legal definition of death says nothing about permanence, it only uses the language of irreversibility, yet permanence is always used in practice.⁶ cDCD NRP follows the essential

elements of permanence—circulation will not restart on its own, and although circulation occurs under the protocol, resuscitation will not be attempted because, in accordance with long-recognized legal and ethical principles, it has been determined to be medically ineffective. This intent behind the decision not to resuscitate is essential to the meaning of permanent cessation. In cDCD NRP, the donor is not resuscitated; the organs are perfused to prepare for donation. Accordingly, the cDCD NRP donor is ethically dead, the dead donor rule is honored, and therefore the law should recognize this.

In addition, because cDCD NRP can better ensure transplantation with good outcomes, it fully honors the donor's wishes, the donor's family's wishes, and the needs of transplant recipients.

ACP states that in cDCD NRP brain death has been caused (by occluding cerebral circulation) to prevent brain reperfusion when circulation is restored.

Occluding cerebral circulation cannot cause brain death because the patient is already dead. The patient has died due to permanent circulatory cessation—circulation has stopped on its own and there will be no attempt to restart it for purposes of saving the donor's life because doing so would be medically ineffective.

Under current standards of cDCD organ donation without NRP (which ACP supports), after the 5-minute hands-off period, the aorta is clamped at the level of the diaphragm or descending thoracic aorta and the body of the deceased is flushed with ice-cold preservation fluid. The brain's ischemic time is thus accelerated. In addition to preventing further warm ischemic injury of the transplantable organs, this maneuver ensures complete cessation of brain function prior to removing the organs. In a similar way, clamping aortic arch vessels in cDCD NRP, after the 5-minute hands-off period, ensures total cessation of brain function before the organs are removed.⁷

According to ACP, the fact that death has already been legally declared by another definition does not mean the declaration cannot be invalidated by subsequent acts.

The law is silent on whether subsequent acts can invalidate a declaration of death. Regardless, occluding cerebral circulation prevents the possibility (however minimal) of neuronal activity creating questions around the circulatory determination of death. But it does not cause death—the patient has already been pronounced dead by standard cDCD criteria.

The goal of cDCD NRP is to ensure that all transplantable organs including the heart are optimally preserved and that the heart is assessed to be sure it will function. In doing so, regional perfusion is implemented with an extra-corporeal pump and oxygenator. Even though this takes 15–20 min on average before blood flow, the brain remains a “black box” and the degree or extent of neuronal death cannot be ascertained. By ensuring that blood flow to the brain remains absent (which began with circulatory arrest) there will be no doubt regarding any degree of coordinated neuronal activity at the time of organ removal.

ACP asserts that NRP resuscitates the patient.

NRP perfuses the body of the deceased. It does not resuscitate the patient.

ACP asks: Is declaring the patient dead by irreversible circulatory criteria, then rendering the patient brain dead before restoring circulation honest, transparent, and respectful of patient autonomy and dignity?

In normal cDCD, which the ACP position statement supports, strict legal brain death requirements—irreversible cessation of all brain function—have almost certainly not been met. Even after the required “hands off” period, there is likely still some amount of uncoordinated neuronal activity. Recovering organs at this moment is honest, transparent, and respectful of patient and family wishes because death has been declared in an ethical way—circulation has stopped and will not be restarted to try to save the patient because this would be medically ineffective.

The same is true for cDCD NRP—circulation will not be restarted; instead, the body of the deceased will be perfused. Brain perfusion is occluded to ensure that random post-mortem brain activity does not cast doubt on the part of the family or any caregiver over the determination of death.

Allowing the deceased and family to fully realize their altruism and gift of organ donation is wholly honest, transparent, and respectful of patient autonomy and dignity.

ACP mentions how more drug overdose deaths might lead to more cDCD. They then say this could “disproportionately affect an underserved and/or stigmatized population...” and ask whether this fulfills the requirements of justice for equitable distribution of benefits and burdens.

How organs are recovered in accordance with the wishes of the donor and their family has no bearing on the medical care received by patients, how people die, or their cause of death.

Choosing not to honor organ donation wishes or choosing not to give these families this option not only does nothing to stem the overdose epidemic, but it denies the possibility of fulfilling altruistic wishes and a desire to bring meaning to an untimely death, which might be the only good that can come from such tragedies.

Transplantation can and does save the lives of people from the same disadvantaged communities where, often, the burden of disease is greater.

ACP states that “If patients or family members of both the donor and recipient are not made aware of the full details of what this protocol involves, this lack of transparency can damage trust in health care and clinical research.”

cDCD NRP recovery is innovative. Standards for communicating about specific actions and practices are still evolving. In discussing with families there is no agreed-upon standard of care regarding how much detail needs to be presented (as is true for all organ and tissue recovery). However, all questions asked by families must be addressed to their satisfaction and comprehension. The emerging area of cDCD NRP authorization of donation requires further study with input from diverse communities to understand how best to respect family interests. This is especially true based on the confusion around and misconceptions about death preceding organ donation.

ACP suggests that we can just use ex-situ perfusion devices and avoid the above-described ethical concerns.

These devices should be used when they are available, and when there are trained staff to operate them. However, there are not enough devices or staff for all potential cDCD donations, which could leave the expressed desire to donate unfulfilled and create inequities based on resources and geography. One significant benefit to cDCD NRP is that it can increase the number of lives saved with much lower resource expenditure.

Additionally, *ex-situ* devices do not allow for an equally thorough evaluation of the function of the heart because they cannot elucidate whether the heart is capable of maintaining hemodynamic stability *in situ*, as is done in cDCD NRP.

Preliminary data from *ex-situ* perfusion suggests that the suitability of hearts for transplant is more difficult to assess (leading to some organ offers being declined), and primary dysfunction of the graft after transplant is higher leading to more morbidities and adverse effects in the recipient.^{8,9} Beyond the heart, cDCD NRP likely provides significant clinical superiority of other transplantable organs by limiting warm ischemic time, which could mean better outcomes for patients.¹⁰

1 | CONCLUSION

The public conversation around the ethics of cDCD NRP is necessary. The concerns expressed by the American College of Physicians help publicize the discourse, but its conclusions against cDCD NRP rest on faulty premises. cDCD NRP does not violate the dead donor rule; it respects the rule the same as traditional cDCD, which ACP supports. cDCD NRP does not cause brain death, but instead ensures cessation of neuronal activity as does cold flushing pursuant to traditional cDCD. While the legal definition of death should be updated to reflect current practice for all circulatory death determinations, the donor in cDCD NRP is declared dead in accordance with the permanence standard for circulatory cessation. cDCD NRP does not resuscitate the patient, but instead perfuses the organs of the deceased for purposes of organ preservation. cDCD NRP can best honor the donation wishes of the deceased and family members by facilitating assessment and recovery of optimal organs for transplant. As with any innovative transplant protocol, cDCD NRP must be accompanied by public education and methodical communication. Discussion with family members must be honest and transparent, respecting their right to know morally relevant facts as well as their right not to know the specific information that would be too clinical or burdensome. The most effective and appropriate means for communication must continue to be refined with input from diverse communities. This input, along with the range of possible DCD NRP techniques, should be considered in a consensus forum to develop recommendations for practice integration. cDCD NRP is one powerful method to expand the supply of optimal organs widely practiced in several other countries and not yet available to

US citizens in need; its benefits far outweigh the addressable ethical considerations raised against the practice.

DISCLOSURE

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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